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10/077,210	02/14/2002	Chung-Hsiun Wu	13062-004001	3095

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EXAMINER	
SAUNDERS, DAVID A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
077,210	WU et al
Examiner	**Group Art Unit**
SAUNDERS	1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 1–26 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 1–22, 25–26 is/are rejected.

☑ Claim(s) 23–24 is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Attachment(s)

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other _____

Office Action Summary

The claims pending and under examination are 1-26.

Claims 1-17, 20-22 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, line 9 "to thereby isolate the fusion protein" is unclear because there is no indication of what this is isolated from. Is it isolated from the sample?

In claim 2, it is unclear as to where in the sequence of steps of claim 1, the further step of "clearing" occurs.

In claims 10-12 it is unclear as to where in the sequence of steps in claim 1, the further step of "immobilizing" occurs and as to how this immobilizing is operative in achieving the overall purpose of the method.

In claim 20, it is unclear as to whether the first or the second amino acid sequence, or both, that "the antibody response" of claim 18 is directed against. It is also unclear how the "first member of a specific binding pair" is operative in method of claim 18.

In claims 16 and 26 are unclear as to where, in sequence of steps of base claims 1 and 18, the step of "removing a B-cell" occurs. It is suggested that applicant conclude these claims, as in the "wherein" clause of claims 15 and 25.

Claims 1-17 and 20-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly

connected, to make and/or use the invention. Applicant's method lacks enablement because the claims leave out an essential step.

In claim 1, between the binding and the administering steps, applicant has failed to recite the essential step of dissociating/releasing the first member of the specific binding pair (sbp) from the second member of the specific binding pair. Note L0 et al. (5,726,044) teach (Example 4) that, when an IL-2 Fc – gamma 1 fusion protein (in which the Fc-gama –1 portion serves as a first sbp) is purified by binding to solid phase Protein A (which serves as the second sbp), the fusion protein must be dissociated and eluted from the solid phase Protein A.

The examiner finds applicant's claims and specification devoid of any teaching, or even hint, of such a step of dissociating the fusion protein from the second sbp member.

Alternatively, it may be considered that the first amino acid sequence of the fusion protein could be released from the second amino acid sequence via cleaving, e.g. as taught by applicant at page 11, lines 6-10. While instant claim 2 refers to a cleaving step, the claim fails to state where, in the sequence of steps recited in claim 1, this cleaving step, sequence of steps recited in claim 1, this occurs; claim 2 is thus properly included in the enablement rejection.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 18 and 25-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Reid (6,054,632).

Reid teaches the production of two transgenic animals. The first of the transgenic animals expresses one allelic from of a given protein (e.g. red cell antigen FY A), while the second transgenic animal expresses another allelic **form** of the same protein (e .g. FYB). A blood sample can be collected from either of the transgenic animals and used to "cross-immunize" the other. Such an immunization incurs production of anti-allotopic (e.g. anti-FY*A or anti-FY*B) antibodies. See Fig. 6, for example.

Instant claim 18 encompasses the method of Reid because:

1) The administering of a nucleic acid and expressing of the encoded protein in a first mammal corresponds to the construction of a transgenic animal expressing an allelic form of a protein. An isolated nucleic acid encoding an allelic form of the protein is administered to a zyyote (see col. 9, line 46 – col. 10, line 10). Applicant's disclosure has not limited the life-stage of the "first mammal" in any way; thus microinjection of DNA into a mammal at the zyyote stage is encompassed by the claim.

2) The removing from the first mammal of a biological sample that contains the protein corresponds to obtaining a blood sample from the first

transgenic animal and isolating the RBCs therefrom. The RBCs contain the expressed allelic form of the protein (e.g. Fy*A or Fy*B) in their membranes.

3) The administering of the protein to a second mammal corresponds to using the RBCs to cross-immunize the second transgenic animal. See Example 5.

Claim 26 is included because Reid teaches production of hybridomas that produce monoclonal antibodies. See Fig. 6 and Example 7.

Claim 25 is included because Reid's teachings of antibody production are not limited to monoclonal antibodies (col. 2, line 16). Also, determining "antibody titres" (col. 12, line 66) would be immediately envisioned as involving obtaining antisera.

Claims 1, 3, 6, 8, 10-11, 13 and 17-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Nemazee (5,698,679).

Nemazee teaches production of nucleic acids encoding fusion proteins, which comprise two segments – an immunoglobulin segment and an inserted (usually in the CDR1 of the L chain) antigenic/epitopic peptide segment. These correspond, respectively, to instant "second" and "first" segments. Such nucleic acid segments can be used to produce transgenic animals (col. 18, lines 1+). As noted supra instant claims do not limit the life stage of the "first mammal" and thus encompass administration to zygotes. Thus the first step of instant claims 1 and 18 is shown by Nemazee.

Nemazee discloses removing B cells from an immunized transgenic mammal – e.g. from spleen/nodes (col.18, lines 26+). This constitutes obtaining a "sample from the first mammal" and is consistent with applicant's description of the sample at page

10, line 2. This spleen cell "sample" contains the expressed fusion protein, as required by instant claims, because B cells within the sample express the fusion protein. Thus Nemazee shows the second step of claims 1 and 18.

Nemazee then cultures the B cells of the "sample" according to conventional hybridoma techniques (col. 18, lines 26+). This step is not contemplated by applicant but is permitted due to claim recitation of "comprising".

Nemazee then recovers supernatant of the culture. He teaches that, after recovery, one may purify the fusion protein by affinity chromatography – e.g. with an antibody that binds immunoglobulin Fc region (col. 17, lines 35+). In such a method the Fc-region of the fusion protein corresponds to the instant "second member of the specific binding pair". Thus the third step of instant claim 1 is shown, as are the features of claims 18-20.

Nemazee utilizes his isolated fusion proteins to generate an antibody response against the inserted antigenic segment (corresponding to applicant's "first amino acid sequence"). See, for example, col. 18, line 37- col. 20, line 42. Thus the last step of claims 1 and 18 is shown.

Claims 3, 6, 8 and 21 are clearly encompassed by the above disclosure of Nemazee.

Regarding claims 13 and 22, note Nemazee's teaching of the length of the antigenic peptide insert at col. 7. lines 3-28.

Regarding claims 10-11, use of affinity chromatography (col. 17, line 48+) inherently involves immobilization of the fusion protein. Note also col. 25, lines 57+ teaching use of columns of Protein A or G to bind the immunoglobulin containing fusion protein.

Claim 17 is rejected because such an affinity chromatography method removes components that are not bound to the "second member of the specific binding pair".

Claims not rejected supra over Reid or Nemazee are allowable over prior art of record. Applicant should more exactly recite his invention to overcome these references.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Vernachio et al. (6,462,254) are cited as of interest for teaching production of fusion proteins in genetically engineered animals. The protein of interest (corresponding to applicant's first amino acid sequence) is fused to a capture tag sequence (for purification) and a detection tag sequence (for assays). The fusion protein may be obtained from a sample from the animal (col. 11, lines 27+). The proteins of interest include therapeutic proteins, but not antigens for immunization (col. 8, lines 58+).

The references of record are considered to teach away from administering a nucleic acid encoding a fusion protein to a first mammal and then isolating the encoded fusion protein from the first mammal for administration to a second mammal. The intermediate step of isolating the fusion protein from the first mammal would be expected to not be necessary, since the prior art teaches that administering the nucleic acid should be sufficient to induce the immune response in the first mammal, and that the process of isolating the fusion protein from a sample from the first mammal would be wastefull of time and effort.

In this regard note teachings of Kikly et al. (6,146,845)at col. 10, lines 55+. Note Felner et al. (5,703,055) at col. 7, lines 37+; col. 19, line 35-col. 22, line 40; and col. 42, lines 16+.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, Ph.D., whose telephone number is (703) 308-3976. The examiner can normally be reached on Monday-Thursday from 8:00 a.m. to 5:30 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A Saunders

D. A. Saunders:jmr
October 8, 2003

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644